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Research Article

A comparative study of *in vivo* antidiabetic activity, histopathology evaluation and gene expression studies in fruit and root crude methanolic extracts of *Momordica charantia* (L)., and *Momordica dioica* (Roxb)

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ABSTRACT

Different parts of *Momordica charantia* and *Momordica dioica* are well known for their medicinal value. The present study aimed to evaluate the antidiabetic activity of crude methanolic fruit and root extracts of *M. charantia* and *M. dioica* in Alloxan induced diabetic male wistar rats. After dissecting the animal's collected liver, pancreas, and kidney, similarly studied the hepatic Notch2 gene expression in control, diabetic, and treated rats. Correspondingly we observed the glucose levels of control, diabetic, treated rats and positive control glibenclamide *Momordica dioica* root showed low glucose levels compared with other tested samples. In the same way, we studied, the pancreas of the *Momordica charantia* treated after diabetes is showing two folds up regulated Notch2 gene expression than *Momordica dioica* root extract. Whereas in kidney, Notch2 gene expression levels of *Momordica charantia* and *Momordica dioica* roots showed three folds up-regulated Notch2 gene expression. *Momordica charantia* root shows three folds Notch2 gene expression upregulated than *Momordica dioica* root extract. Histopathological studies also indicate severe aberration was seen in positive control and *Momordica dioica* fruit, but no tissue degeneration was normal in *Momordica charantia* fruit and root. Our findings suggest that Methanolic crude fruit and root extracts of *Momordica charantia* and *Momordica dioica* possess antidiabetic properties. Further, we can conclude that the medicinal plants *Momordica charantia* and *Momordica dioica* could be used to develop natural drugs to cure diabetes.

Keywords: *In vivo*, Antidiabetic activity, *M. charantia*, *M. dioica*, Notch2 gene, Histopathology

INTRODUCTION

Diabetes Mellitus (DM), one of the most common endocrine related metabolic disorders, has caused significant morbidity and mortality. Due to microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular (heart attack, stroke, and peripheral vascular disease) complications [1,2]. According to WHO projections, the prevalence of diabetes is likely to increase by 35% year by year. Currently, there are over 150 million diabetic patients worldwide, and this is likely to increase to 300 million or more by the year 2025. India's statistical projection suggests that diabetics will rise from 15 million in 1995 to 57 million in 2025, the highest number of people with diabetes globally [3-5]. Reasons for this rise include an increase in sedentary lifestyle, consumption of with the most significant diabetics are Asia and Africa, where diabetes mellitus rates could rise twofold to threefold than the present rates [6]. Plant based medicine has been used cost effectively worldwide to treat diabetes. In fact, in many parts of the world, impoverished countries may be the only form of therapy available to treat diabetic patients. Different authors have several reviews about antidiabetic herbal plants [7-10].

Momordica species have their place in the vegetable crops belonging to the family of cucurbitaceae (also commonly referred to as cucumber, gourd, melon, or pumpkin family), which comprises medium sized plants that grow abundantly in warmer regions all over the world. They are well known for their bitter taste due to phytochemicals (alkaloids) and have a wide range of medicinal values. Even though the exact origin of the *Momordica* genus is unclear, most experts agree that the

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center of bitter gourd domestication lies in eastern Asia, possibly eastern India or southern China. Different plant parts of *Momordica* are branded for their bioactive compounds, phenols, flavonoids, carotenoids, triterpenoids, and phytosterols. The phytochemicals found in *Momordica* species have received ample attention in the recent literature. They mainly focused on the potential health benefits of compounds with high antidiabetic, antitumor, and antioxidant properties. In particular, some actual scientific research trends are intensely focused on obtaining *in vitro* evidence for the biological efficacy of individual constituents such as triterpenoids, carotenoids, and phenolics from different parts of *Momordica* spp. Approximately 228 bioactive compounds were found from different parts of *M. charantia* [11,12]. *Momordica* dioica is a climbing creeper and is considered an essential medicinal herb from ancient times used to treat many headaches, urinary calculi, jaundice, asthma, bronchitis, leprosy, and fever, tumors, urinary discharges, excessive salivation, and heart problems [13,14]. There are few reports related our work but there is no evidence for comparative analysis of *in vivo* antidiabetic activity of fruits and roots crude extracts of *M. charantia* and *M. dioica* methanolic fruit and seeds extracts. Taking lacuna into consideration, in this study, we attempted to test the *in vivo* antidiabetic activity of fruits and roots crude extracts of *M. charantia* and *M. dioica*. However, some reports are there on *in vivo* antidiabetic activity of fruits and roots of crude methanolic extracts of *M. charantia* and *M. dioica* separately. But here, we attempted to compare the ability of *M. charantia* and *M. dioica* fruits and roots as an antidiabetic agent. Surprisingly, this study also studied the expression of the hepatic Notch2 gene after treating the fraction in diabetic rats. In Pancreas, *Momordica charantia* is showing two folds up-regulated expression rather than *Momordica dioica* root extract. In kidney, Notch2 gene expression levels of *Momordica charantia* and *Momordica dioica* roots were compared. *Momordica charantia* root shows three folds up regulated expression rather than *Momordica dioica* root extract.

MATERIALS AND METHODS

Collection of plant material

Diseased free fresh plant parts *viz.* fruits and roots of *M. charantia* and *M. dioica* were collected from the Adilabad district, Telangana state.

Preparation of extracts

Collected fruits and roots of *M. charantia* and *M. dioica* were washed thoroughly under running tap water, shade dried in open air separately, and then powdered of the samples obtained by grinding them mechanically. About 100 gm of each dried powder of the plant were soaked apart in 100 ml of methanol in conical flasks and then subjected to agitation on a rotary magnetic shaker for about 72 hours. After three days, the plant extracts were subjected to filtration, filtered separately with No 42 what man filter paper. Concentrated extracts were preserved in sterilized air tight labeled bottles and well maintained in the refrigerator at 4^{o}C until required for further use.

In vivo antidiabetic activity

Animals

Wistar rats (8–10 weeks) were obtained, and the study was conducted from the animal house facilities of Jeeva life sciences, uppal industrial area, Hyderabad with animal ethical committee certified protocol CPCSEA/IAEC/JLS/005/02/16/00 2. Earlier and throughout the experiment, rats were fed with the standard diet. After randomization into various groups and before initiation of the study, the rats were acclimatized for 7 days under standard animal house conditions like temperature, relative humidity and dark/light cycle.

Experimental design

The rats were fasted for 8 hours and were treated with Alloxan to induce diabetic condition was by injecting at a dose of 25 mg/m1 for one rat. The antidiabetic property studies were conducted for the seven groups, and each group consisted of 6 rats. Glibenclamide standard (1 mg/one rat), positive control (Alloxan 25 mg/one rat), negative control and 4 test compounds (*M. charantia* fruit, root, and *M. dioica* fruit and root). Animals were given a dose once in a day for 30 days period at same time intervals. Each rat was administered intraperitoneally with 250 mg/ kg body weight alloxan (prepared freshly in citrate buffer (50 mM, pH 3.0) for three consecutive days. After one week administration of first dose, random blood glucose levels were estimated using a portable glucometer. Rats that had hyperglycemia (blood sugar level>300 mg/dl) were selected for further experimentation. At the end of each treatment programme rats were sacrificed by chloroform asphyxiation and cervical dislocation. Blood and tissues were collected and stored at–80^{o}C until further analysis.

Group I: Rats were given an oral dose of 0.5 ml per one rat (200-250 gm) body weight of methanolic extract of *Momordica charantia* root.
Group II: Rats were given an oral dose of 0.5 per one rat (200-250 gm) body weight of methanolic extract of *Momordica charantia* fruit.
Group III: Rats were given oral dose of 0.5 ml per one rat (200-250 gm) body weight of methanolic extract of *Momordica dioica* root.
Group IV: Rats were given oral dose of 0.5 ml per one rat (200-250 gm) body weight of methanolic extract of *Momordica dioica* fruit.
Group V: This group served as negative group no drug.
Group VI: This group served as positive group induced Alloxan monohydrate 25 mg per one rat.
Group VII: This group served as standard group treated with Glibenclamide 1 mg/ml.

Histopathology

The liver, kidney, and pancreas from each animal were removed after sacrificing the animal and collected in 10% formalin solution and immediately processed by the paraffin technique. Sections of 5 thicknesses were cut and stained by haematoxylin and eosin (HE) for Histological Examination.

Gene expression studies

Isolation of total RNA

Total RNA from frozen liver tissue will be isolated with the RNeasy mini kit (Qiagen, Stanford, CA). Samples will be processed following the manufacturer's directions. At the last step, the RNA will be eluted with 50 µl of RNase free water. Quality of the RNA will be assessed using Agilent.

RT-PCR (q-PCR)

We adopted classical method of RNA extraction procedure was using Trizol. Avoided DNA contamination an extraction kit containing DNase was used. Obtained RNA measured by using Nanodrop and cDNA was reverse transcribed by a Superscript III syn thesis kit (Takara, Tokyo, Japan). Gene expression assay was carried out using standardized SYBR green in a 7900HT fast real time PCR system (Applied Biosystems). Comparative quantitation analysis was performed using the delta Ct (2–ΔCt) method with β-actin and GAPDH as the endogenous controls, normal and treated organs *viz* liver, kidney, and pancreas as calibrator. Primers were prepared from Qiagen.

Gel electrophoresis

Assessment of PCR products will be carried out using agilent bionalayzer system. The PCR product will be visualized as a single compact band with expected size.

RESULTS

Animals were sacrificed for 30 days and made devoid of blood to enable clear organ structure by dislocating jugular vein or carotid artery. The organs were (liver, kidney and pancreas) collected and consign to histopathology after the gross pathological examination. Since our last reports revealed, analyzed, and reported the comparative analysis of phytochemical differences between both fruit and root extracts of *M. dioica* and *M. charantia* proving that the presence of various medicinally important preliminary phytochemicals. The fruits and roots of both plants were extracted separately with methanol, ethanol, water, and petroleum ether chloroform and screened for their phytochemical constituents.

Antidiabetic activity

The antidiabetic study was carried in male wistar rats in the body weight range of 200–250 gm at the time of initiation. The anti-diabetic property studies were randomly divided in to the 7 groups each group consisted 6 rats. The rats were render diabetic using negative control alloxan (25 mg/ one rat) except normal rat. Glibenclamide standard (1 mg/ml), positive control and 4 groups fruit and roots methanolic extracts of *Momordica charantia* and *Momordica dioica*. The rats were fasted for 8 hours and were treated with alloxan diabetic was induced by injections at a dose of 25 mg/m1 for one rat. Animals were dosed once in a day for duration of 30 days. Glucose levels were determined on day 0, 8, 15, 21 and 30th day. The results are compiled in a tabular form for the comparison. Methanolic extracts of fruits and roots of *Momordica charantia* showed notable antidiabetic activity from day 21st till the end of the study when compared with positive control glibenclaminde. Whereas *Momordica dioic*a fruit showed low antidiabetic activity compared with the above two compounds from day 21. Astonishingly the *Momordica dioica* root showed hyperglycemic activity. The antidiabetic activity continued till the end of the study 30 day. The positive and negative controls showed the glucose level as per expectations (Table 1).

Table 1: The positive and negative controls showed the glucose level as per expectations**.**

S. No	Groups	Mean ± SD Day 0	Day 8	Day 15	Day 21	Day 30
1	*Momordica charantia* root	492.16 ± 63.177	434.66 ± 57.301	401.666 ± 77.036	240.666 ± 37.302	131 ± 10.583
2	*Momordica charantia* fruit	516.333 ± 54.117	472.5 ± 71.840	443.333 ± 75.513	250.5 ± 41.181	139 ± 5.059
3	*Momordica dioica* root	554 ± 54.203	510.8 ± 50.687	486 ± 70.873	471.333 ± 101.962	473.333 ± 109.714
4	*Momordica dioica* fruit	548 ± 60.089	464.333 ± 52.098	452.6 ± 69.478	323.5 ± 80.293	258.5 ± 36.391
5	Positive control	95.666 ± 9.395	93.166 ± 5.036	94.833 ± 3.311	96. ± 3.687	94.166 ± 6.968
6	Negative control	547.5 ± 56.641	500.4 ± 45.511	526.66 ± 33.620	474.66 ± 71.444	475.666 ± 80.884
7	Control	512.5 ± 60.718	462.833 ± 50.783	407.6 ± 63.52	297 ± 121.220	150 ± 13.019

Histopathologic studies

The histopathological data of the kidney, liver and pancreas supported and is in concurance with the blood glucose levels of the rats with the various treatments. The order of the methanolic plant extracts in controlling the blood glucose levels in induced diabetic rats also showed the comparative normal and degenerative tissues of the organs under study kidney, liver and pancreas. *Momordica charantia* has been used for treatment of diabetes for centuries. Charantin a natural steroidal glycoside present in the fruits of this medicinal plant has been reported to possess potential hypoglycemic activity. However, this phytoconstituent has not been explored yet clinically to treat diabetes. This review summarizes the chemistry, biological activity and reported analytical methods for charantin a bioactive compound present in *M. charantia* [15].

Momordica charantia fruit used for the treatment of diabetes and hypoglycemic effects of various postulated mechanisms. However, clinical trial data with human subjects are limited and flawed by poor study design and low statistical power. The present review is an attempt to highlight the antidiabetic activity as well as phytochemical and pharmacological reports on *M. charantia* and calls for better designed clinical trials to further elucidate its possible therapeutic effects on diabetes. *Momoridica dioica* fruit extract in Alloxan induced diabetic wistar rats. Aqueous extract of *Momoridica dioica* showed maximum fall (52.8%) in 0 to 1 h fasting blood glucose in tolerance test compared to the present study antidiabetic activity and histopathalogy evaluation of *Momordica charantia* and *Momordica dioica* fruit and roots of methanolic extracts in Alloxan induced forty two male wistar rats has been taken up to carry out. The results are compiled in a tabular form for comparison. No antidiabetic activity was seen till day 15. *Momordica charantia* fruit and roots of methanolic extracts showed antidiabetic activity from day 15 till the end of the study when compared with standard compound (glibenclaminde). *Momordica dioica* root showed low antidiabetic activity compared with the above two compounds from day 21. *Momordica dioica* fruit has showed very low antidiabetic activity. The antidiabetic activity continued till the end of the study that is 30 days. The positive and negative controls showed the glucose levels as per expectations. That validates the study and the screening criteria. Comparative analysis of glucose levels in methanolic extracts of *Momordica charantia* and *Momordica dioica* fruits and roots. Kidney tissues in the control group showed normal renal corpuscles. But some morphological and pathological changes occurred in the kidney tissues of diabetic control Wistar rats treated with methanol extracts of *Momardica charantia* and *Momordica dioica* fruit and root extracts. The glomerular region of the kidney, some atrophic changes and haemolysis were seen but cellularity and basement membrane were normal. No inflammatory cells were found. The tubular portion also showed atrophic chsianges, shedding of epithelium and oedema. Liver in normal animal showed normal hepatic cells with well preserved cytoplasm, nucleus, nucleolus and central vein. In diabetic control liver section showed the lobular architecture that was maintained but there were also severe fatty changes, sinusoidal dilation and congestion, mild periportal inflammation, fibrosis, severe feathery degeneration and necrosis. The diabetic rats treated with *Momardica charantia* and *Momordica dioica* fruit and root methanolic extracts. Liver section maintained lobular architecture and had mild fatty change, mild sinusoidal dilation and congestion, mild periportal inflammation and mild feathery degeneration.

Pancreas showed normal islets, beta cells appeared normal in the islets. Acinar cells appeared normal in pancreas. Degeneration, inflammation and necrosis noticed in entire non glandular pancreas. Periductular fibrosis, thickening of ductular region of glandular pancreas. Mild to moderate degenerative changes and haemorrahages noticed in glandular pancreas. Mild ductular epithelial cells hyperplasia noticed (Figure 1).

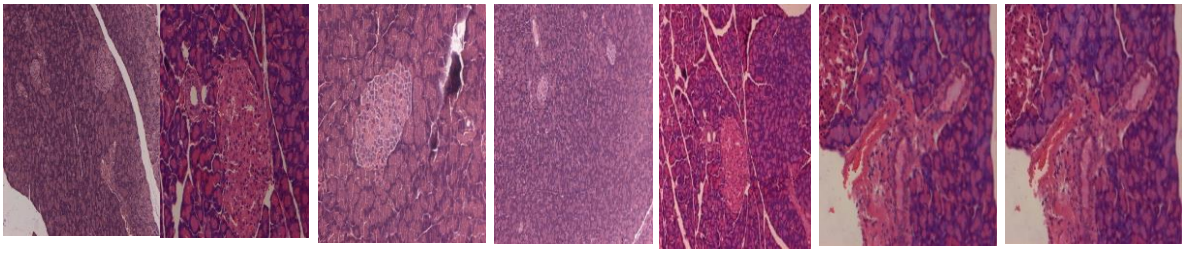

Figure 1. Histopathology of pancreas with various treatments.

- Islets of pancreas appeared normal; no degeneration noticed.
- Beta cells appeared normal in the islets. Acinar cells are appeared normal in the pancreas. Glandular pancreas containing islets cells appeared normal. Collecting ducts in the glandular pancreas apeared normal. Acinar cells population appeared normal in non-glandular region of pancreas. No degeneration, inflammation and necrosis noticed in entire non glandular pancreas.
- Islets of langerhansappeard normal. Beta cells in the islets are appeared normal, No degeneration notuiced in the cells. Acinar cells in the pancreas appeared normal, no degeneration or inflammation noticed.
- Glandular pancreas containing islets cells appeared normal collecting ducts in the glandular pancreas appeared normal. Acinar cells population appeared normal in non-glandular region of pancreas. No degeneration, inflammation and necrosis noticed in entire non glandular pancreas.
- Periductular fibrosis sin which thickening of ductularregon of glandular pancreas. Moderate to severe ductular fibrosis along with proliferation of ductular epithelial cells (Figure 2). Moderate degeneration of islets cells in glandular pancreas.
- Mild to moderate degenerative changes.

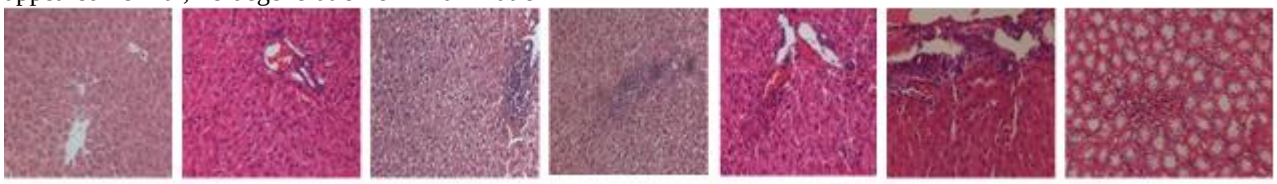

Figure 2. Histopathalogy of liver with various treatments.

- Hepatocytes appeared normal red arrow, Portal vein appeared normal black arrow. Portal triad containing blood vessels and bile ducts appeared normal.
- Portal triad containing portal vein along with bile ducts appeared normal. Hepatocytes appeared

normal in entire liver (portal, periportal and centribular region). No degeneration, inflamation and haemorrhages noticed.

- Moderate inflammation along with infiltration of inflammmatory cells noticed in peri portal region of liver arrow. Peri portal inflammation noticed mild.
- Most of the hepatocytes appeared normal but mild peri vascular infiltratoin of inflammatory cells noticed arrow. Mild, few foci of necrosis of hepatocytes noticed arrow.
- Portal triad containing portal vein along with bile duct appeared normal. Hepatocytes appeared normal in entire liver (portal, peri portal and centrilobular region). No degeneration, inflammation and haemorrhages noticed.
- Moderate to severe hyperplasia of billary epithelial cells noticed in the portal region of liver. Moderate to severe peri portal inflammation with infiltration of inflammatory cells particularly lymphocytes noticed in the liver.
- Hepatocytes appeared normal in entire liver (portal, peri portal and centrilobular region). Portal triad containing portal vein and bile duct appeared normal. No degeneration or inflammation noticed in entire liver (Figure 3).

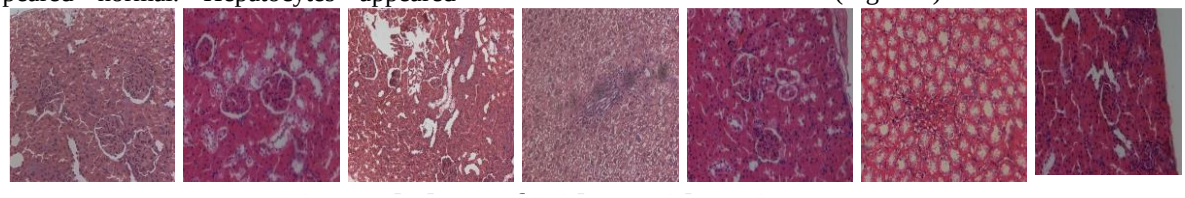

Figure 3. Histopathalogy of kidney with various treatments.

- Glomerulusappered normal tubular region appeared normal no degeneration/inflamation noticed.
- Glomerillus region appeared normal Tubular region appeared normal capsular region appeared normal no degeneration, inflamation noticed in the glomerillus and tubular region.
- Moderate tubular degeneration noticed in the entire kidney glomerillus appeared normal.
- severedelitition of tubules noticed in the kidney. Moderate interstitial nephritis in which interstitium between the tubular regions are infammed along with infiltration of inflamattory cells noticed.
- Tubularregion, glomerulus region and capsular region appeared normal in kidney. No inflamation noticed in the glomerulus and tubular region. No degeneration noticed in the glomerulus and tubular region.
- Tubularhaemorrhages and infiltration and inflamatory cells noticed in the collecting ducts of kidney.
- Moderate multifocal tubular nephritis or tubular inflamation noticed in the cortex and medullary region of kidney.
- Mcr=*Momordica charantia* root
- Mcf=*Momordica charantia* fruit
- Mdr=*Momordica dioica* root
- Mdf=*Momordicadioica* fruit
- Nc=Negative control
- Pc=Positive control
- Std=Standard

Gene expression studies

Q-PCR result revealed that insulin, glucokinase, Pdx 1, PTP 1b gene expressions were upregulated. *M. charantia* treated animals gained body weight. Rats treated with *M. charantia* gained weight, two way ANOVA (p=.1769). It is a fact that insulin is involved in regulating the metabolism of biomolecules through induction of the absorption of glucose from the blood into liver, fat, and skeletal muscle cells. As the first enzyme in the glycolysis pathway, glucokinase can phosphorylate glucose to trap it in the cells. Protein Tyrosine Phosphatase 1B (PTP1B) is an enzyme involved in regulating the insulin signaling pathway. Finally, we verified the insulin expression with immunocytochemistry and noted more and larger pancreatic islands in treated rats. Collectively, q-PCR data indicate the reversion of pancreas gland function to normal. The liver is among the organs that are affected directly as diabetes progress. To explore the role and integrity of the liver, we analyzed the liver enzyme activity and its histology. Interestingly, when animals were exposed to *M. charantia* at 20% concentration, their liver GOT, GPT, and ALP enzyme activities returned to normal levels compared to untreated one (p=.0022). No significant changes in enzyme activity were observed between 10% and 20% *M. charantia*. *M. charantia* in doses of 10% and 20% showed the protective effects at liver of treated diabetic rats compared to untreated diabetic rats.

In this experiment, Wistar rats were fed with two plant root extracts of *Momordica charantia* and *Momordica dioica* in different doses, and rats were sacrificed on the 37th day. Pancreas and kidney tissues were freshly collected and stored in liquid nitrogen till the experiment. RNA was isolated using the Trizol reagent, converted to cDNA, and further used for Notch2 gene expression studies. In Pancreas, *Momordica charantia* is showing two folds up regulated expression rather than *Momordica dioica* root extract. Whereas in kidney, Notch2 gene expression levels of *Momordica charantia* and *Momordica dioica* roots were compared in which *Momordica charantia* root is showing three folds up regulated expression rather than *Momordica dioica* root extract (Figures 4-7).

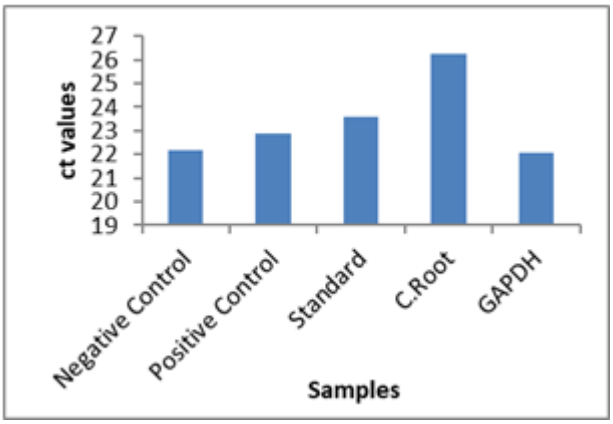

Figure 4. Gene expression levels of pancreas in *Momordica charantia*. Root showing high expression when compared to standard.

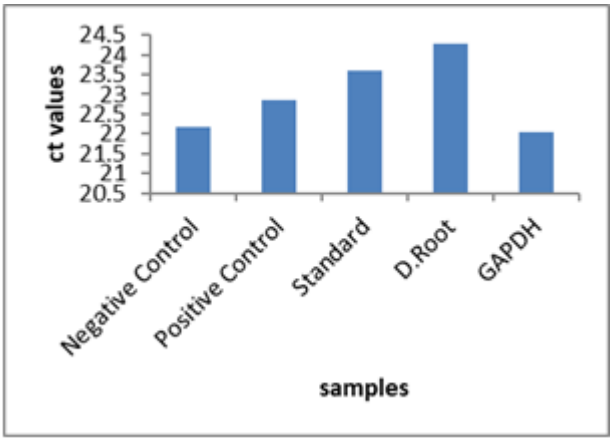

Figure 5. Gene expression levels of pancreas in *Momordica dioica*. Root showing high expression when compared to standard.

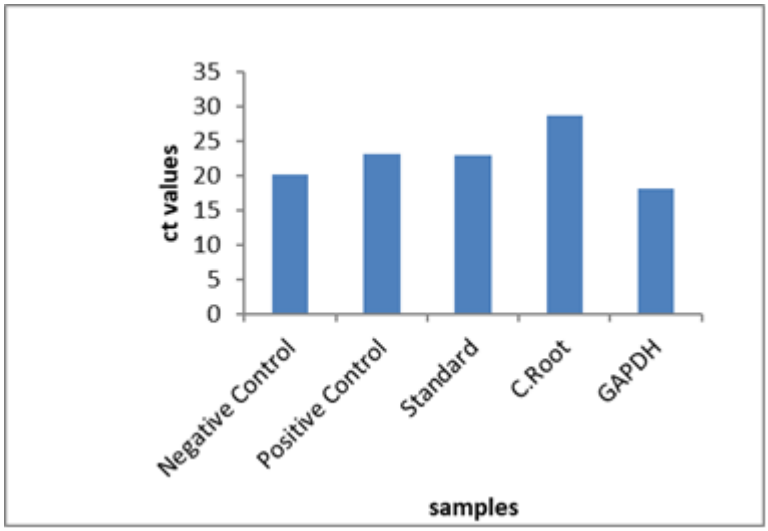

Figure 6. Gene expression levels of kidney in *Momordica charantia* root showing high expression when compared to standard.

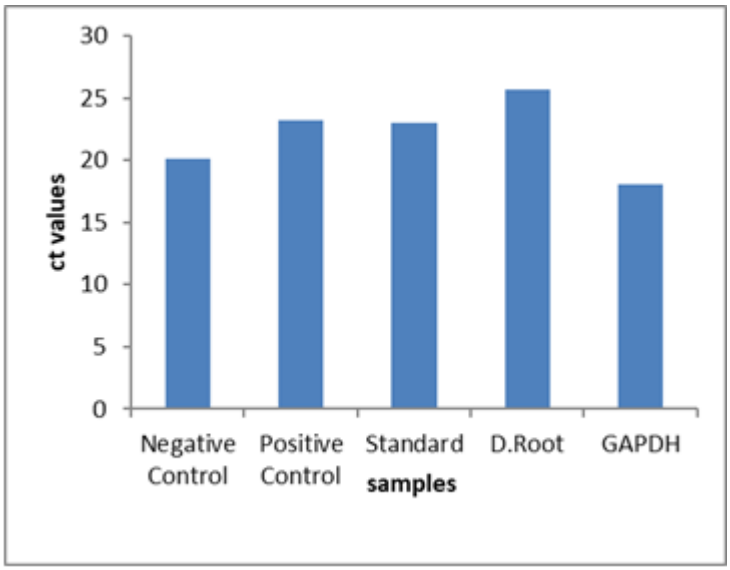

Figure 7. Gene expression levels of kidney in *Momordica dioica* root showing high expression when compared to standard.

DISCUSSION

The phytochemical constituents present in the plants plays an important role in the identification of new crude drugs. Phytochemical screening is very significant for identification of new sources of therapeutically and industrially important compounds like alkaloids, flavonoids, phenolic compounds, saponins, steroids, tannins, terpenoids etc., reported that isolated phytochemicals revealed the presence of various activities. Terpenoids are reported to have analgesic, antioxidant and anti-inflammatory activities. Flavonoids are the large class of plant pigments has a structure similar to flavone are reported to possess many useful properties like anti-inflammatory, antidiabetic activity, oestrogenic, antimicrobial, anti-allergic, antioxidant, and anti tumour activity. Anthocyanins provide protection to humans against viral infections by improving their immune system. Glycosides and alkaloids have shown hypoglycemic activities. Tannins act as an anti-fungal, anti-bacterial and antiviral agent [16]. Saponins contains valuable medicinal properties and widely used as detergents, pesticides and foaming agent in industries and surface active agents. Phenols known to have great importance as germicidal, antiseptic agent [17] and they can able to protect human from oxidative stress which may cause numerous disease, including cancer, cardiovascular problems and ageing [18].

Exicisting data suggests that the Notch gene encodes a transmembrane receptor that gave the name to the evolutionary highly conserved Notch signaling cascade. It plays a pivotal role in the regulation of many fundamental cellular processes such as proliferation, stem cell maintenance and differentiation during embryonic and adult development [19]. After specific ligand binding, the intracellular part of the Notch receptor is cleaved off and translocates to the nucleus, where it binds to the transcription factor RBP-J. In the absence of activated Notch, RBP-J represses Notch target genes by recruiting a corepressor complex. And Notch signaling with a focus on gene regulatory events at Notch target genes [20]. This is of utmost importance to understand Notch signaling since certain RBP-J associated cofactors and particular epigenetic marks determine the specificity of Notch target gene expression in different cell types [21]. Also, Notch target genes and the physiological significance of Notch signaling in development and cancer. Our findings indicate the involvement of the Notch pathway in Alloxan induced diabetes mice [22]. Gene expression (RT-qPCR) assessed notch pathway and VEGF involvement in DM-EPCs were assessed by gene expression (RT-qPCR).Our findings indicate the involvement of Notch pathway in mediating DM-EPCs dysfunction and migrated cell number when compared to control. Further *in vitro* inhibition of Notch pathway by GSI rescued DM-EPC dysfunction. Therefore targeting Notch pathway in diabetes mellitus may provide a target to restore DM-EPC dysfunction. There are many studies displayed Notch aberrancies in association with their progress of cancer and disease development, the management of which is still challenging.

CONCLUSION

The usage of medicinal plants is a unique ancient traditional practice. Due to their immense value in conventional medicine, medicinal plants need to be evaluated for their potency. There is an urge to assess the mechanism of their significant pharmacological accomplishment and their allied welfares and adverse properties. Hence, the practice of herbal medicines is still persistent in present society for the anticipation, safety, welfare also management of diabetes. Even commercially formed drugs are primarily derived from plants, and it's a boom for present day modern medicine.

Consequently, various medicinal herbs and plants showed antidiabetic activity by regulating insulin secretion, insulin sensitivity to the cells, glucose abruption, etc., to improve glycemic control. However, there are many reports to prove various plants as an antidiabetic agent. But we need scientific validation testing protocols in order to evaluate the quantity and quality of active principles for herbal drug formulation. Based on the impression of medicinal plants as an antidiabetic agent in the present study, we progress to evaluate antidiabetic activity of *Momordica dioica* root, fruit and *Momordica charantia* root, fruit. With this, our current study revealed that the pancreas of the *Momordica charantia* treated after diabetes is showing two folds up regulated Notch2 gene expression than *Momordica dioica* root extract. Wherever in kidney, Notch2 gene expression levels of *Momordica charantia* and *Momordica dioica* roots

showed three folds up regulated Notch2 gene expression. *Momordica charantia* root shows three folds Notch2 gene expression upregulated than *Momordica dioica* root extract. Histopathological studies also indicate severe aberration was seen in positive control and *Momordica dioica* fruit, but no tissue degeneration was observed in *Momordica charantia* fruit and root. We conclude that methanolic crude fruit and root extracts of *Momordica charantia* and *Momordica dioica* possess anti-diabetic properties. Further, we can recommend that the medicinal properties of *Momordica charantia* and *Momordica dioica* could be used to develop herbal medicine to cure diabetes.

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